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Hepatology Highlights

Hin Hin Ko;[1] Eric M. Yoshida[2,3]

Efficacy of Triple Therapy with Thymalfasin, Peginterferon alpha-2a, and Ribavirin for the Treatment of Hispanic Chronic Hepatitis C, Nonresponders by Poo JL *et al.*

Hepatitis C (HCV) is the worldwide leading cause of liver cirrhosis and hepatocellular carcinoma. The goal of treatment is to prevent complications and achieving a sustained virological response (SVR). Various factors, such as genotype, viral load, ethnicity, and fibrosis scores, correlate with the likelihood of patients achieving an SVR. Patients with genotype 1, high viral loads, cirrhosis or pre-cirrhosis on biopsy and failures to previous therapy, are very difficult to treat and often have the greatest clinical need. Therefore, new therapeutic options and more efficacious treatment strategies are desperately needed. Thymalfasin is a pure, synthetic amino-terminal acylated peptide of 28 amino acids that can trigger maturational events in lymphocytes, augment T cell function, promote reconstitution of immune defects, and inhibit viral replication. Compared to IFNá monotherapy, thymalfasin and IFNá had been shown to have higher rates of biochemical, virological and histological responses.

In this issue, Poo et al. evaluated the efficacy and tolerability of 48-week triple therapy with thymalfasin, peg-IFNα-2a and ribavirin in 40 patients, of Hispanic demographic background, with chronic HCV who were non-responders to previous IFN-α/ribavirin treatment, as defined by no virologic response at the end of at least 6 months of IFN-α/ribavirin therapy. At 12 weeks, 57.5% experienced a >2log$_{10}$ drop in HCV RNA and 52.5% were RNA negative (< 600 IU/mL). 52.6% showed an end-of-treatment response at week 48 and 21.2% achieved a SVR (23.5% of genotype 1 achieved SVR). Normalization of ALT was also seen in 30% at week 12 and 37% at week 72, respectively.

This study suggests that thymalfasin, in combination with peg-IFNα-2a and ribavirin, may have a potential role in difficult-to-treat HCV non-responders. However, one should keep in mind that the study sample size is small and the results may not be generalizable to other patient populations. It is also important to note that there was no comparator group (ie. control group). Whether thymalfasin would be an effective new therapy in HCV non-responders still needs to be confirmed by larger, randomized trial. Furthermore, it would be interesting to see studies comparing the efficacy of thymalfasin with other exciting new therapies such as albinterferon alpha-2b,[1] protease inhibitors (e.g. telaprevir[2,3] and boceprevir[4]), and polymerase inhibitor (R1626)[5] in the treatment of hepatitis C. Those agents have been shown to have substantial antiviral effect in treatment-naïve patients with genotype 1; however, their efficacy in non-responders is yet to be determined.

Non-Alcoholic Fatty Liver Disease in Severely Obese Individuals: The Influence of Bariatric Surgery by de Andrade AR *et al.*

Together with the worldwide obesity epidemic, the incidence of the metabolic syndrome is rising. It is a complex condition that is linked to obesity and is characterized by insulin resistance, dyslipidemia and hypertension. Non-alcoholic fatty liver disease (NAFLD) is the primary hepatic complication of obesity and insulin resistance. Without treatment, NAFLD can progress to liver cirrhosis and hepatocellular carcinoma. Currently there is no effective treatment for NAFLD; therefore, weight loss achieved through different means (diet, exercise, medications and bariatric surgery) has been promoted as the standard treatment.

In their study, de Andrade *et al.* followed clinical and biochemical parameters in forty obese patients (mean BMI of 45.9 ± 5.7 kg/m^2 and waist circumference 125 ± 17cm) for a mean of 21 ± 5.8 months after bariatric surgery. At baseline, steatohepatitis without fibrosis (NASH) and steatohepatitis with fibrosis were observed in 15% and 80%, respectively. Following surgery, the mean BMI was 29.5 ± 23.0 kg/m^2 and there were statistically significant improvements in all clinical and biochemical parameters, except AST. Significant fewer patients meet the

[1] Chief Fellow, Division of Gastroenterology, University of British Columbia.
[2] Professor of Medicine, Head, Division of Gastroenterology, University of British Columbia.
[3] President, Canadian Association for the Study of Liver.

Address for correspondence:
Dr. Eric M. Yoshida
Division of Gastroenterology
Gordon and Leslie Diamond Health Care Center
5153- 2775 Laurel Street. Vancouver, BC
V5Z 1M9, CANADA
E-mail: Eric.Yoshida@vch.ca

criteria for metabolic syndrome post-op (12.5% vs. 27.5%) and insulin resistance was also only found in 2.5% of patients (vs. 66.7% pre-op). However, no liver biopsies were performed after the surgery and thus histological comparisons could not be made.

This study showed promising improvements in conditions associated with NAFLD; however, these are only surrogate endpoints and may not necessarily reflect significant histological improvements. At present, lifestyle modification should be attempted first and medical therapies can be used in adjunct. A few studies have appear to demonstrate that medications such as insulin-sensitizing agents, lipid lowering drugs, antihypertensive drugs and antiobesity agents are effective treatment for NAFLD. Bariatric surgery might be an effective therapy for NAFLD if the above measures fail in those with significant obesity refractory to conventional management. Furthermore, the decision should be individual based and the benefits and risks of the procedure should be discussed with the patient. Longer-term studies are still warranted to assess for potential relapse of NASH/NAFLD that could result with weight gain or malnutrition as a possible consequence of the surgery.

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